REMARKS

This application pertains to a novel abuse-proofed dosage form.

Claims 1, 2, 4, 7, 8, 27- 29, 31, 41 and 42 are pending.

The title is being corrected because the file history reflects the word "proofed" in the title as being spelled both correctly as -proofed-- and incorrectly as "proffed". Even the filing receipt reflects the incorrect spelling of the word. By this amendment the title is corrected to reflect the correct spelling of the word "proofed". It should be noted that the word is spelled correctly in all the claims.

I. Objection to Claim 41

Claim 41 stands objected to because the Examiner views the claim identifier of "Previously presented" to be incorrect and believes that the identifier should have read "currently amended". However, claim 41 was not amended in the last response, and therefore "Previously presented" was the correct identifier. Claim 42, on the other hand, *was* amended and the identifier for that claim should have read "currently amended". It appears that the amendment was entered, so it would therefore be improper to identify that claim in the present response as "currently amended" since no further amendment is currently being made.

In order to provide a properly-identified set of claims, Applicants' have provided a listing of claims in this response, wherein claim 42 is identified as "Previously presented", on the assumption that the earlier amendment was entered and in view of the fact that no further amendment is being made presently. Despite the fact that no amendments are being made presently, the claims are being presented just so that the

record will reflect a properly-identified set of claims.

In view of the foregoing, the objection to claim 41 should be withdrawn.

II. Alleged Obviousness of the Claims

Claims 1, 2, 4, 7, 8, 27-29, 31, 41 and 42 stand rejected under 35 U.S.C. 103(a) as obvious over Oshlack et al (US 2003/0064099/A1) in view of DOW Technical Data, POLYOX™ WSR, February 2003.

A. Dow is now removed as alleged Prior Art.

It is respectfully pointed out that the accompanying counterpart Rule 131 Declarations antedate the DOW reference, thereby obviating the rejection.

B. Oshlack relates to fundamentally different technology and the combination of Oshlack and Dow does not make out a *prima facie* case of the obviousness of any of the rejected claims.

In addition to the fact that the DOW reference is no longer available against the present claims, and the rejection is thereby obviated, the following comments show that even if the DOW reference was available against the present claims, the combination of Oshlack and DOW would not render Applicants' claims obvious.

The Oshlack reference pertains to a controlled release dosage form which includes aversive agents, such as a bittering agent or a viscosity increasing agent, which make abuse unpleasant, but do not in any way render the dosage form abuse-proofed. Oshlack contemplates that his dosage forms may be crushed or chewed. See paragraphs [0067 - 0068], where it is disclosed that Oshlack's aversive agents are

"released" when the dosage form is e.g. chewed. Thus, Oshlack ***discourages***, but does not necessarily prevent abuse. Oshlack's dosage forms ***must*** be tampered with in order to perform their intended function, i.e., to release the aversive agents. If somehow Oshlack's dosage forms were rendered crush-proof, as Applicants' dosage forms are, then Oshlack's point of novelty would be destroyed, and his dosage forms could not perform their intended function.

All of Oshlack's embodiments require that his dosage forms be capable of being chewed or crushed.

In all embodiments, Oshlack manifests his "less abuse potential" by building-in aversive agents that are released when the dosage form is tampered with, and these aversive agents render the abuse unpleasant thereby discouraging abuse.

Although Oshlack precedes everything he says about his dosage forms with the expression "In certain embodiments", the fact is that the entire Oshlack disclosure is directed towards dosage forms that release aversive agents when tampered with.

Although the Oshlack reference includes language that "in certain embodiments" his dosage forms comprise aversive agents that are released when the dosage forms are tampered with, and that "tampering" includes e.g. crushing, chewing etc., nowhere is there to be found in Oshlack any "embodiment" whatsoever that is not susceptible to such "tampering". Clearly all of Oshlack's dosage forms are susceptible to crushing or chewing so as to release the aversive agents.

There is absolutely nothing in Oshlack pertaining to any dosage forms that **could *not*** be crushed or chewed. Any dosage form that could not be crushed or chewed would render Oshlack's invention inoperable. Should the Examiner disagree, she is

respectfully asked to point out where in Oshlack she sees any dosage form that cannot be crushed or chewed?

In the office action, at page 6, the Examiner contends that "If the prior art teaches the composition, then the properties are also taught by the prior art." As discussed further below, the prior art does not teach or suggest the claimed composition. Even if Applicants' *composition* could be found in some combination of references, it would be technically incorrect to conclude that the properties, namely the breaking strength of at least 500N, are "inseparable from the composition." In this regard, the Examiner is respectfully invited to compare the "properties" of a diamond to the "properties" of a lump of coal. The two have the same composition but yet have vastly different properties. These result from the different process that the two have been subjected to.

Applicants' achieve their high breaking strength by press-forming their dosage form with the simultaneous or preceding application of heat (paragraphs [0067] and [0117]). The dosage composition being compressed is heated to at least the softening temperature of component (C) [0067].

Oshlack does not disclose any such treatment for any dosage forms that remotely approach the composition of Applicants'.

Oshlack, at paragraph [0111], indicates that his dosage form may be produced by melt-extrusion and/or pressed into tablets.

However, the composition that is melt extruded in paragraph [0111] does not comprise Applicants' polyalkylene oxide (C). Note that in Oshlack's paragraph [0111] Oshlack's melt extrusion involves melting e.g. a wax and incorporating a powdered drug therein. In order to obtain "sustained release," Oshlack teaches that it may be

necessary to incorporate a hydrophobic sustained release material, such as ethyl cellulose or a water insoluble acrylic polymer into the molten wax hydrophobic binder material, and refers to US 4,861,598 for examples of sustained release formulations prepared by melt-granulation techniques. This patent concerns base materials which are combinations of acrylic resins with higher aliphatic alcohols.

Nowhere is there any disclosure or suggestion of any compositions having a breaking strength of at least 500N, or of any technique whereby such a breaking strength might be obtained, or even the desirability of such a breaking strength. To the contrary, Oshlack is specifically directed to dosage forms that are susceptible to "tampering" and which release the aversive agents upon such tampering. Accordingly, Oshlack teaches away from Applicants' novel abuse-proofed dosage forms.

Applicants' claims require that the breaking strength of Applicants' dosage form be at least 500 N. The Oshlack reference clearly teaches away from such a breaking strength in that it is an essential character of Oshlack's oral dosage form that it be chewable...see Oshlack's paragraph [0055]. Such chewing is essential in order for Oshlack's aversive agent to be released. If Oshlack's dosage form could not be chewed, the aversive agent would not be released and Oshlack's mechanism for discouraging tampering with the dosage form would not be realized.

As can be seen from the previously submitted publication Proeschel, *J Dent. Res 81* (7):464-468, 2002, the mean human chewing force is about 200 N, which means that the breaking strength of Oshlack's dosage form must be no more than about 200 N; otherwise it could not be chewed and the aversive agent could not be released.

Moreover, Applicants' claims require that the active ingredient be present in a controlled release matrix of polyalkylene oxide having a molecular weight of 1-15 g/mol.

Oshlack et al. mentions polyalkylene oxide having a molecular weight of at least 0.5 million. Nevertheless, the only disclosure of these polymers is exclusively concerned with osmotic dosage forms (Oshlack et al., [0148]-[0159]), which, however, are not sintered.

In another context, Oshlack et al. mentions methods for the preparation of matrix formulations which methods may be regarded as thermoforming, such as melt-extrusion (Oshlack et al., [0111]). These matrix materials according to Oshlack at al., however, do not encompass polyalkylene oxides (Oshlack et al., [0097]).

Furthermore, in the dosage form according to claim 1 of the present application, the active ingredient is present in a controlled-release matrix of component (C). The active ingredient is embedded in the high molecular weight polyalkylene oxide that in turn serves as a retardant agent (specification, page 35, lines 13-19).

In contrast thereto, the release profile of the osmotic dosage forms according to Oshlack at al. does not rely on a controlled-release matrix, but on the expansion of the waterswellable high molecular polyalkylene oxides in the push layer, which does not contain the drug.

In other words, in the dosage forms according to the subject invention the high molecular weight polyalkylene oxide serves as a controlled-release matrix thereby retarding the release profile of the drug. In contrast thereto, in the osmotic dosage forms according to Oshlack et al., a semi-permeable membrane hinders the drug from being released and the swelling of the high molecular weight polyalkylene oxide rather causes

the drug to leave the dosage form by pushing it through an orifice in the semipermeable membrane.

Therefore, the effect of the high molecular weight polyalkylene oxide in the matrix dosage forms of the present invention and in the osmotic dosage forms of the Oshlack reference are directly opposite to each other.

Further, Applicants' claims are limited to the use of polyethylene oxide having a molecular weight of 1-15 million, according to rheological measurements. Oshlack mentions the use of polyethylene oxide as a gelling agent, but does not teach or suggest anything about the use of polyethylene oxide having a molecular weight of 1-15 million. As can be seen from the previously submitted product description sheets the chemical supplier SIGMA-ALDRICH® commercializes polyethylene oxides having molecular weights of 10,000 g/mol and 100,000 g/mol, respectively, i.e. molecular weights which are 10 times and 100 times lower than the lower limit according to instant claim 1. Accordingly, Oshlack's disclosure of the use of polyethylene oxide as a gelling agent does not teach or suggest anything about the inclusion of polyethylene oxide in the 1-15 million molecular weight range as a hardening agent.

Further yet, Applicants' dosage forms require that the polyalkylene oxide be present in an amount sufficient to result in a breaking strength of at least 500 N. As shown by the previously submitted Rule 132 declaration, lesser amounts of polyethylene oxide did not achieve Applicants' breaking strength.

There is nothing in the reference that would teach or suggest anything about even the possibility of achieving such a breaking strength under any circumstances, let

alone any hint that this could be achieved by including a sufficient amount of polyalkylene oxide and sintering.

Still further, Oshlack et al. is not a broad general disclosure containing a vast number of features that a skilled person would readily combine with one another, but a disclosure of distinct dosage forms having distinct properties based on distinct excipients and distinct processes of manufacture.

Oshlack et al. contains various sections dealing with different concepts of pharmaceutical technology by which to realize different dosage forms, each section containing a separate heading, e.g.:

coated beads [0084]

matrix formulation [0096]

osmotic dosage forms [0148]

transdermal delivery systems [0160]

suppositories [0168].

A skilled person is fully aware that each section deals with another type of dosage form. A skilled person would not follow the Examiner's approach to arbitrarily pick individual features that are only disclosed in connection with a particular type of dosage form and combining them with other features disclosed in connection with other particular types of dosage forms.

The dosage forms according to the present invention can be regarded neither as coated beads, nor as osmotic dosage forms, nor as transdermal delivery systems nor as suppositories.

Rather, the dosage forms according to the present invention can be regarded as matrix formulations where the polyalkylene oxide having a molecular weight of 1-15 million g/mol forms a matrix in which the active ingredient is embedded.

According to Oshlack et al., however, polyethylene oxide is not among the matrix materials disclosed therein.

In this regard, Oshlack et al. merely discloses:

> **[0097]** A non-limiting list of suitable sustained-release materials which may be included in a sustained-release matrix according to the invention includes hydrophilic and/or hydrophobic materials, such as gums, cellulose ethers, acrylic resins, protein derived materials, waxes, shellac, and oils such as hydrogenated castor oil and hydrogenated vegetable oil. However, any pharmaceutically acceptable hydrophobic or hydrophilic sustained-release material which is capable of imparting sustained-release of the opioid analgesic may be used in accordance with the present invention. Preferred sustained-release polymers include alkylcelluloses such as ethylcellulose, acrylic and methacrylic acid polymers and copolymers; and cellulose ethers, especially hydroxyalkylcelluloses (especially hydroxypropylmethylcellulose) and carboxyalkylcelluloses. Preferred acrylic and methacrylic acid polymers and copolymers include methyl methacrylate, methyl methacrylate copolymers, ethoxyethyl methacrylates, ethyl acrylate, trimethyl ammonioethyl methacrylate, cyanoethyl methacrylate, aminoalkyl methacrylate copolymer, poly(acrylic acid), poly(methacrylic acid), methacrylic acid alkylamine copolymer, poly(methylmethacrylate), poly(methacrylicacid) (anhydride), polymethacrylate, polyacrylamide, poly(methacrylic acid anhydride), and glycidyl methacrylate copolymers. Certain preferred embodiments utilize mixtures of any of the foregoing sustained-release materials in the matrix of the invention.

In fact, the entire section dealing with matrix formulations according to Oshlack et al. is completely silent on polyalkylene oxide having a molecular weight of 1-15 million g/mol.

Analogously, as the section dealing with matrix formulations according to Oshlack et al. is the only section mentioning hot-melt extrusion technique - which the Examiner "considers" as a sintering method (Oshlack et al., [0111]-[0129]), the feature combination {polyalkylene oxide + hot melt-extrusion/sintering}, let alone the feature combination {polyalkylene oxide having a molecular weight of 1-15 million g/mol + hot-melt extrusion/sintering} cannot be derived from Oshlack et al.

Those skilled in the art understand that hot-melt extrusion and sintering are two entirely different concepts, and that the morphology of a dosage form prepared by hot-melt extrusion differs from the morphology of a sintered dosage form according to the present invention. The Examiner's contention that "The melt-extrusion technique of Oshlack et al encompasses the sintering technique of the instant claims..." is totally without merit. Those skilled in the art are well aware of melt-extrusion, and no person skilled in the art would ever argue that melt-extrusion encompasses "sintering". These are two different concepts, and neither encompasses the other.

The only disclosure of Oshlack et al. concerning polyethylene oxide having a molecular weight within the range of instant claim 1 of the present application is in connection with delivery or push layers of osmotic dosage forms (Oshlack et al., [0150]-[0151]).

Said delivery or push layers of osmotic dosage forms, however, do not contain the drug. Instead, in osmotic dosage forms the drug is contained in a drug layer that is separate from said delivery or push layer.

Accordingly, in the osmotic dosage forms according to Oshlack et al. the drug is not present in a controlled release matrix of the polyethylene oxide having a molecular weight of 1-15 million g/mol.

In addition, there is no hint in Oshlack et al. of any osmotic dosage forms prepared by hot melt-extrusion. Thus, also when starting from this section of Oshlack et al., the combination {polyalkylene oxide + hot melt-extrusion }, let alone the feature combination {polyalkylene oxide having a molecular weight of 1-15 million g/mol + hot-melt extrusion } cannot be derived, let alone that the opioid is present in a matrix of the polyalkylene oxide or that the dosage form is sintered.

In sum, various arbitrary selections from distinct sections of Oshlack et al. are relied upon by the Examiner in her attempt to arrive at the feature combination of instant claim 1, i.e. that the active ingredient is present in a controlled release matrix of polyethylene oxide having a molecular weight of 1-15 million g/mol.

Such arbitrary selections are contrary to the general technical understanding that would be reached by those skilled in the art from a reading of Oshlack et al. and merely represent an artificial approach based on an attempt at hindsight reconstruction.

The Examiner's attention is respectfully drawn to the following further points:

C. The combination of Oshlack and Dow fails to make out a prima facie case of the obvious of the instantly claimed dosage forms having a breaking strength of at least 500 N.

1. The record is devoid of evidence of motivation of persons skilled in the art, given Oshlack and Dow, to make and use the instantly claimed dosage forms having a breaking strength of at least 500 N.

No person having ordinary skill in the art would have had any reason to combine the teachings of Oshlack and Dow in any manner that could possibly lead to the present invention. Applicants once again respectfully remind the Examiner that "[a]ll words in a claim must be considered in judging the patentability of that claim against the prior art (emphasis added)." See, MPEP § 2143.03, citing In re Wilson, 424 F.2d 1382, 1385, 165 USPQ 494, 496 (CCPA 1970). The instant claims require that component (C) be present in an amount sufficient to result in a breaking strength of said sintered mass of at least 500 N. The record is devoid of any reason why a person having ordinary skill in the art, given Oshlack and Dow, would have been motivated to make a dosage form comprising instant component (C) present in an amount sufficient to result in a breaking strength of said sintered mass of at least 500 N.

(a). The Examiner has only alleged the combination of Oshlack and Dow is proper because both are drawn to sustained release dosage forms, but has not alleged that the combination would be desirable for any sufficiently good reason.

According to the Examiner:

"At the time of the invention it would have been obvious to one skilled in the art to use the POLYOX™ WSR of high molecular weight of [Dow] for the sustained release dosage forms of Oshlack et al. as both disclosures are drawn to sustained release dosage forms having PEO polymers which are used for the preparation of thermoformed tablets (emphasis added)."

However, as stated in MPEP § 2143.01(III):

"The mere fact that references can be combined or modified does not render the resultant combination obvious unless the results would have been predictable to one of ordinary skill in the art (emphasis added)."

Along the same lines is the following explanation from In re Gyurik et al., 201 USPQ 552, 557 (CCPA 1979):

"An element in determining the obviousness of a new chemical compound is the motivation of one having ordinary skill in the art to make it. That motivation is not abstract, but practical, and is always related to the properties or uses one skilled in the art would expect the compound to have, if made (again, emphasis added)."

The Examiner does not indicate any expected/predicted results of her hypothetical combination of Oshlack and Dow. (Absent her acknowledgement of what would have been expected/predicted, it is perhaps not surprising that the Examiner cannot concede the present claims are characterized by unexpected results.)

Certainly, the combination of Oshlack and Dow will have inherent properties. However, it is well settled that what is inherent is not necessarily known, and obviousness cannot be based on what is unknown. See, for example, In re Spormann, 363 F.2d 444, 448, 150 USPQ 449, 452 (CCPA 1966). Consequently, resort to unknown inherent properties, for example, that the resulting dosage form will have a breaking strength of 500 N, cannot provide the basis in the expected/predicted properties of the resultant combination that must be alleged in order for a prima facie case of obviousness to be made out. The Examiner has not made any findings as to the expected/predicted properties of the resultant combination, and, therefore, has not

provided a legally sufficient basis for concluding the requisite motivation to combine the two references in the manner she proposes.

There are two possibilities:

(1) A person having ordinary skill in the art would have been motivated to use Dow's PEO polymer in Oshlack's dosage forms in the expectation of achieving another dosage form that would operate in the manner Oshlack envisions; or

(2) A person having ordinary skill in the art would have been motivated to use Dow's PEO polymer in Oshlack's dosage forms in the expectation of achieving a dosage form having a breaking strength of at least 500 N despite the fact that such a dosage form is not contemplated by Oshlack.

(b). The Examiner has not shown that a person having ordinary skill in the art would have had any reason to expect that a dosage form combining the features of Oshlack and Dow would have a breaking strength of at least 500 N or why, if they had such expectation, such a person would have been motivated to make such a dosage form since such a dosage form is inconsistent with Oshlack's teachings.

Considering possibility (2) first, the Examiner at points appears to be arguing along these lines, writing the following:

"Therefore, at the time of the invention it would have been obvious to one ordinarily skilled in the art that the sustained release dosage forms of the combined references of [Oshlack] and [Dow] contains a high molecular weight PEO polymer in an amount sufficient to result in a breaking strength of at least 500 N (emphasis added)."

In the immediately preceding sentence, the Examiner found:

"Further, the opioid and PEO polymer dosage forms of [Oshlack] contain the PEO polymer in a ratio to the opioid agonist of from about 1:15 to about 15:1 by weight and are prepared via a melt-extrusion technique, which encompasses the sintering preparation process of the instant claims (again, emphasis added)."

Applicants disagree that Oshlack's melt-extrusion technique encompasses the sintering preparation process used to prepare the sintered product of the instant claims.

However, putting that difference aside for the moment, Applicant also disagrees that Oshlack leads persons skilled in the art to the definite use of PEO polymers in the dosage form, or even in an amount that would be required to prepare a dosage form having a breaking strength of at least 500 N.

i. The record is devoid of any reason why persons skilled in the art would have selected polyethylene oxide as Oshlack's gelling agent as opposed to any of the many other gelling agents listed by Oshlack.

The Examiner finds under numbered paragraph 12 on page 4 of the Office Action that Oshlack teaches a sustained release dosage form which comprises "an aversive agent/gelling agent, such as polyethylene oxide." It is true that polyethylene oxide is mentioned as a possible gelling agent in Oshlack's paragraph [0049]. However, the polyethylene oxide is buried in a long list of suitable gelling agents encompassing some 40+ species and genera, which are expressly stated to be "for example and without limitation." See line 4 of paragraph [0049]. As such, this teaching literally covers millions of possible compounds considering just the named species and genera, and who knows how many more compounds considering the "for example and without limitation" language. Further, polyethylene oxide is not listed in any of the preferred

embodiments starting at line 17 of paragraph [0049], nor is polyethylene oxide used in any of Oshlack's working examples. Consequently, Applicants question at the outset: How does a person having ordinary skill in the art led by Oshlack's disclosure choose polyethylene oxide as the gelling agent in the first place?

Applicants respectfully remind the Examiner that although the claimed invention may be within the generic teachings of the prior art, and theoretically could have been achieved with the proper selections, a *prima facie* case of obviousness is not made out unless the prior art highlighted these selections in some manner, and, therefore, led persons skilled in the art towards them. *See, In re Baird,* 29 USPQ2d 1550, 1552 (Fed. Cir. 1994) ("The fact that a claimed compound may be encompassed by a disclosed generic formula does not by itself render that compound obvious.") The Examiner has not pointed to anything in Oshlack that would have led persons having ordinary skill in the art to select polyethylene oxide as the gelling agent from Oshlack's lengthy list for incorporation into a dosage form.

ii. The record is devoid of any reason why persons skilled in the art would have selected polyethylene oxide of molecular weight 1-15 million as the gelling agent, particularly since the Examiner concedes that Oshlack does not teach the molecular weight of the polyethylene oxide.

Further on this point, the instant claims require that component (C) comprises "a polyalkylene oxide having a molecular weight of 1-15 million according to rheological measurements." The Examiner concedes that Oshlack does not disclose a PEO of molecular weight 1-15 million and, also, does not explicitly disclose the dosage form has

a breaking strength of at least 500 N. Applicants further question then is: How does one skilled in the art, given Oshlack, proceed not only to select polyethylene oxide from Oshlack's lengthy list of gelling agents, but also polyethylene oxide of molecular weight 1-15 million, and then gain the expectation of achieving a dosage form having a breaking strength of at least 500 N? And, if the person skilled in the art should somehow make all the right selections, what should he or she expect can be done with such a dosage form, once obtained since such a dosage form is proven by the data of record here to be non-crushable and, therefore, incapable of serving Oshlack's purposes?

Respectfully, Applicants submit that Oshlack does not lead persons skilled in the art to select polyethylene oxide as the gelling agent. Oshlack does not lead persons skilled in the art to select polyethylene oxide of molecular weight 1-15 million for such purposes. Oshlack does not lead persons skilled in the art to expect that a dosage form made from polyethylene oxide of molecular weight 1-15 million will have a breaking strength of at least 500 N, even inherently. And, Oshlack does not suggest that even if such a dosage form could be obtained, it would have any use.

iii. Choosing polyethylene oxide of high molecular weight as the gelling agent, even in a ratio of PEO polymer:opioid of 1:15 to 15:1 does not inherently result in a dosage form having a breaking strength of 500 N, as proven by data already of record.

The Examiner's position seems to be that Oshlack mentions polyethylene oxide as a gelling agent, and also mentions amounts of the gelling agent that overlap the amounts in the instant claims; and if a person having ordinary skill in the art should use

one of the high molecular weight polyethylene oxide polymers of Dow, then such person would inherently obtain a dosage form having a breaking strength of at least 500 N.

Applicants respectfully disagree. First, there is nothing in Dow that directs persons skilled in the art to use higher molecular weight polyethylene oxide (> 1,000,000 Mw) as opposed to lower molecular weight polyethylene oxide (< 1,000,000 Mw). Quite the contrary, Dow suggests the lower molecular weight PEO polymers are easier to process. See, for example, Dow in the first paragraph in the right-hand column on the first page thereof, indicating that the lower molecular weight PEO grades have better flow characteristics than their higher molecular weight counterparts and can be processed using conventional equipment, where the higher molecular weight grades have limited melt flow characteristics and often require plasticizer for successful processing. Accordingly, if persons skilled in the art are led more towards one direction than the other, they are led by Dow to the use of lower molecular weight polyethylene oxide rather than higher molecular weight polyethylene oxide due to the better melt flow and processing characteristics. Consequently, in the combination of Oshlack and Dow, there is nothing to highlight the use of polyethylene oxide as the gelling agent, or, moreover, the use of higher molecular weight PEO polymers for such purpose.

Second, there are data already of record that establish that even when a higher molecular weight PEO polymer is used, the exact amount used is *critical* in achieving the breaking strength of 500 N. The data include amounts within Oshlack's 1:15 to 15:1 ratio, on which the Examiner relies crucially, and prove that simply selecting any amount in this range does not guarantee that the resulting dosage form will exhibit a breaking strength of at least 500 N. Consequently, the Examiner is incorrect that simply because

Oshlack describes a ratio of 1:15 to 15:1 that a person having ordinary skill in the art would have found it obvious that "the sustained release forms of the combined references of [Oshlack] and [Dow] contains a high molecular weight PEO polymer in an amount sufficient to result in a breaking strength of at least 500 N." Selecting an amount within the 1:15 to 15:1 PEO:opioid ratio does not inherently achieve a breaking strength of at least 500 N.

Before addressing the data in detail, Applicants respectfully remind the Examiner that inherency is a strict standard to satisfy. Where, as here, the Examiner relies on a theory of inherency as to any particular element, then the extrinsic evidence must make clear that such element is ***necessarily*** present in the thing described in the reference, and the presence of such element therein would be so recognized by persons skilled in the art. *In re Robertson,* 49 USPQ2d 1949, 1950-51 (Fed. Cir. 1999). Further, inherency is not established by probabilities or possibilities, and the mere fact that a property ***may*** result from a given circumstances is not sufficient; instead it must be shown that such property ***necessarily*** inheres in the thing described in the reference. *Id.*

Now, Applicants call the Examiner's attention again to the Declaration of Dr. Heinrich Kugelmann executed February 6, 2009, which was filed as an attachment to the amendment after final filed February 17, 2009. The declaration reports the results of breaking strength comparisons of oxycodone HCl tablets prepared using polyethylene oxides at various molecular weights and amounts. The tabulated data are reproduced below for the Examiner's convenience, adding a new row for the PEO:opioid polymer ratio:

[mg]	A-1	A-2	B-1	B-2	C-1	C-2
Oxycodone HCl	20.0	130.00	20.0	130.0	20.0	130.0
Polyethylene oxide						
M_w 600,000 g/mol	130.0	20.0				
M_w 5,000,000 g/mol			130.0	20.0		
M_w 7,000,000 g/mol					130.0	20.0
Total weight	150.0	150.0	150.0	150.0	150.0	150.0
Ratio PEO: oxycodone HCl	**6.5:1**	**1:6.5**	**6.5:1**	**1:6.5**	**6.5:1**	**1:6.5**
Breaking Strength [N]	>500	**<500**	>500	**<500**	>500	**<500**

The Examiner should note that all of the compositions tested fell within Oshlack's PEO: opioid ratio of 1:15 to 15:1. Yet, simply being within that range did not guarantee a breaking strength of at least 500 N, as ***three*** of the embodiments (A-2, B-2 and C-2) did ***not*** achieve a breaking strength of at least 500 N in spite of the fact that the PEO:opioid ratio was within Oshlack's range. Applicants respectfully submit that these data prove that it is not necessarily the case that selecting Dow's high molecular weight PEO and formulating the PEO:opioid ratio within Oshlack's ratio will yield a dosage form having a breaking strength of at least 500 N. Consequently, the Examiner is simply incorrect that because Oshlack describes a ratio of 1:15 to 15:1 that a person having ordinary skill in the art would have found it obvious that "the sustained release forms of the combined references of [Oshlack] and [Dow] contains a high molecular weight PEO polymer in an amount sufficient to result in a breaking strength of at least 500 N."

Further, embodiments B-2 and C-2 involved higher molecular weight PEO polymers, showing even the selection of such polymers in amounts within Oshlack's PEO:opioid ratio of 1:15 to 15:1 does not guarantee a breaking strength of at least 500 N.

Along the same lines are the data submitted in the Declaration of Dr. Johannes Bartholomäus executed August 25, 2008, which was also filed as an attachment to the

amendment after final filed February 17, 2009. The declaration reports the results of breaking strength comparisons of tramadol HCl tablets prepared using polyethylene oxides at various molecular weights and amounts. The data are reorganized below for the Examiner's convenience, with an added column for the PEO:opioid polymer ratio:

Ex.	Ingredient	[wt.-%]	PEO:tramadol HCl ratio	Breaking Strength [N]
3	Tramadol HCl	45.00	1:1.28	>500
	Polyethylene oxide M_w 100,000	35.00		
4.1	Tramadol HCl	35.00	1:1.75	**<500**
	Polyethylene oxide M_w 200,000	20.00		
4.2	Tramadol HCl	25.00	1:1.25	>500
	Polyethylene oxide M_w 200,000	20.00		
4.3	Tramadol HCl	25.00	2.2:1	>500
	Polyethylene oxide M_w 200,000	55.00		
4.4	Tramadol HCl	20.00	3:1	>500
	Polyethylene oxide M_w 200,000	60.00		
5.1	Tramadol HCl	50.00	1:10	**<500**
	Polyethylene oxide M_w 5,000,000	5.00		
5.2	Tramadol HCl	45.00	1:3	>500
	Polyethylene oxide M_w 5,000,000	15.00		
5.3	Tramadol HCl	45.00	1:1.28	>500
	Polyethylene oxide M_w 5,000,000	35.00		
5.4	Tramadol HCl	25.00	2.2:1	>500
	Polyethylene oxide M_w 5,000,000	55.00		
5.5	Tramadol HCl	5.00	16:1	>500
	Polyethylene oxide M_w 5,000,000	80.00		
6	Tramadol HCl	24.90	2.2:1	>500
	Polyethylene oxide M_w 7,000,000	55.00		

Once again, the data prove that simply because the ratio of PEO:opioid is within Oshlack's ratio range of 1:15 to 15:1 does not guarantee that even the use of a high

molecular weight PEO polymer will yield a dosage form exhibiting a breaking strength of at least 500 N. Thus, Examples 4.1 and 5.1 have such ratio, but the dosage forms produced therefrom did ***not*** exhibit a breaking strength of at least 500 N.

Further, embodiment 5.1 involved a higher molecular weight PEO polymer, once again showing even the selection of such polymers in amounts within Oshlack's PEO:opioid ratio of 1:15 to 15:1 does not guarantee a breaking strength of at least 500 N.

Simply put, a breaking strength of at least 500 N is not inherent in Oshlack's PEO:opioid ratio range of 1:15 to 15:1 even if applied to Dow's higher molecular weight PEO polymers.

iv. As a breaking strength of 500 N is not inherent even in the combined teachings of Oshlack and Dow, and as Oshlack and Dow are both silent about such breaking strength, the record does not provide any explanation or other evidence of motivation why persons skilled in the art would have been motivated to prepare dosage forms expected to have a breaking strength of 500 N, particularly when such dosage forms are inconsistent with Oshlack's principle of operation.

Applicants respectfully submit that the Examiner has not advanced any good reason for a person having ordinary skill in the art, given Oshlack and Dow, to manipulate the choice and/or the amount of PEO polymer to produce a dosage form having a breaking strength of at least 500 N. As noted above, the Examiner concedes that Oshlack is silent about a breaking strength of at least 500 N. Applicants have

proven in the specification and in the declarations of record that the inventive dosage forms having a breaking strength of at least 500 N cannot be crushed by ordinary means available to an addict, for example, they cannot be crushed with a hammer. This non-crushability is the essence of the present invention, the fundamental principle on which the present invention operates. An addict cannot chew or crush the inventive dosage form by means ordinarily available to him/her to gain access to the opioid contained therein. The non-crushability of the inventive dosage form, thus, provides the proofing against abuse.

Oshlack operates on a diametrically opposing fundamental principle. Oshlack takes full advantage of the manner in which addicts chew or crush the dosage forms to liberate the opioid contained therein. Oshlack incorporates aversive agents in the dosage forms. Oshlack intends that the addict will proceed, as he or she normally does, to chew or crush the dosage form and, when this happens, then Oshlack's incorporated aversive agents will be released, thereby discouraging the addict from taking further steps in the abuse cascade. Thus, the ability of the Oshlack's dosage form to be chewed crushed by ordinary means available to the addict is an essential component of Oshlack's operating principle. If the dosage form cannot be chewed or crushed by ordinary means available to the addict, then Oshlack's aversive agents contained therein cannot be released, and cannot function in the intended manner to discourage the addict from taking further steps toward abuse.

Applicants respectfully submit that no person having ordinary skill in the art, given Oshlack, and understanding the principle upon which Oshlack operates, i.e., chewing or crushing of the dosage form is needed to release aversive agents contained

therein, would have been motivated to make a dosage form having a breaking strength of at least 500 N, which, therefore, cannot be chewed or crushed by means ordinarily available to an addict, and, thus, could not release Oshlack's aversive agents in accordance with Oshlack's fundamental principle of operation.

In this regard, Applicants refer the Examiner to *MPEP* § 2143.01(V), entitled "**The Proposed Modification Cannot Render the Prior Art Unsatisfactory for It's Intended Purpose**"; and to *MPEP* § 2143.01(VI), entitled "**The Proposed Modification Cannot Change the Principle of Operation of a Reference**." Applicants respectfully submit that the Examiner's proposed combination of Oshlack and Dow, to the extent the Examiner theorizes that a person having ordinary skill in the art would have been motivated to make a dosage form having a breaking strength of at least 500 N, violates both of these basic principles of patent law and, therefore, is presumptively improper.

In re Gordon, 221 USPQ 1125 (Fed. Cir. 1984), cited and discussed therein, was a case where the Patent Office quite literally tried ***to turn the prior art on its head.*** The involved claims related to a blood filter assembly device that required that both blood inlets and outlets be located at the ***bottom*** of the device, and a gas vent was located at the top of the assembly. Such construction was essential for the device to operate as envisioned by the inventors. The cited prior art taught a liquid strainer for removing dirt and water from gasoline, wherein the inlet and outlet were at the ***top*** of the device, and a stopcock was located at the bottom of the device. The prior art reference taught the dirt and water removal was assisted by gravity, thereby fixing the inlet and outlet at the top. Superficially, the prior art device appeared similarly constructed to the claimed device, albeit turned upside down. On appeal, the Board

concluded that the claims were *prima facie* obvious over the prior art, reasoning that it would have been obvious to turn the prior art device upside down, as no patentable distinction was created by the viewing the prior art device from one direction as opposed to another.

The Federal Circuit disagreed, holding:

> "The mere fact that the prior art could be so modified would not have made the modifications obvious unless the prior art suggested the desirability of the modification.
>
> "Indeed, *if the [prior art] apparatus were turned upside down, **it would be rendered inoperable for its intended purpose.*** * * * In effect, [the prior art reference] teaches away from the board's proposed modification (emphasis added)."

See, Gordon, 221 USPQ at 1127.

Here too, the Examiner seeks to turn the Oshlack reference on its head. Where Oshlack clearly contemplates a dosage form that can be chewed or crushed by means ordinarily available to an adduct so that aversive agents contained therein can be released and work to discourage the addict from taking further steps towards abusing the opioid contained therein, the Examiner apparently finds it would have been obvious to dispense with Oshlack's principle of operation and make a dosage form so strong that it cannot be chewed or crushed by the ordinary means available to an addict and, therefore, also could not release Oshlack's aversive agents to thereby discourage abuse of the opioid contained therein in the manner that is the fundamental principle underlying Oshlack's invention. Applicants respectfully submit that such a theory is not

a proper rationale for an obviousness rejection, as evidenced by *MPEP* § 2143.01(V & VI), and *Gordon,* as such a theory changes Oshlack's principle of operation and, moreover, renders the prior art unsatisfactory for Oshlack's intended purposes.

D. The claimed dosage forms exhibit unexpected properties, and operate by a completely new principle not previously known, and, therefore, are nonobvious, as a matter of law.

1. Because there is no reason to expect that the instant dosage form should have a breaking strength of 500 N, and nothing in the combination of Oshlack and Dow to suggest that such a dosage form has advantages in discouraging opioid abuse, the present claims are characterized by unexpected results that are objective evidence of nonobviousness.

Returning to possibility (1) above, i.e., that a person having ordinary skill in the art would have been motivated to use Dow's PEO polymer in Oshlack's dosage form in the expectation of achieving another dosage form that would operate in the manner Oshlack envisions, Applicants respectfully submit that if this is the motivation to combine the teachings of Oshlack and Dow, then the present invention is characterized by unexpected results, as evidenced once again by the data of record. As noted above, Oshlack's fundamental principle of operation is that his dosage forms, and, therefore, also the combined Oshlack/Dow dosage form, should be chewable and crushable by ordinary means available to an addict so that tampering therewith releases the aversive agents contained therein, discouraging the addict from taking further steps at abusing the opioid contained therein. Nothing in the combination of Oshlack and Dow teaches or suggests non-crushable, non-chewable dosage forms that provide abuse-proofing

not by the release of aversive agents, but principally by virtue of their extreme breaking strength, and the inability of the addict to crush them by ordinary means and, thus, to access the opioid contained therein. Accordingly, Applicants' dosage form, which is not crushable or chewable in the manner Oshlack envisions, but yet still provides abuse-proofing by a fundamentally different means of being so strong, having a breaking strength of at least 500 N, that an addict cannot crush it by ordinary means available to them, must be considered to be surprising and unexpected in view of the combination of Oshlack and Dow, and, therefore, also unobvious.

(a). Evidence of record establishes that conventional dosage forms, like Oshlack's, do not have a breaking strength of at least 500 N, and, therefore, also that Applicants' dosage forms are a novel type of dosage form, discouraging abuse by an entirely new approach.

Applicants refer to the Declaration of Dr. Johannes Bartholomäus, executed May 3, 2007, which was filed as an attachment to the amendment filed May 29, 2007. In particular, Applicants draw the Examiner's attention to numbered paragraph 5 thereof, which reads as follows:

> "A breaking strength of 500 N is ***far above*** the typical breaking strength of conventional pharmaceutical forms. Conventional dosage forms typically have breaking strengths ***well below 200 N*** (emphasis added)."

This evidence establishes the novel and fundamentally different nature of Applicants' inventive dosage forms, and stands unrebutted by any evidence the Examiner has offered.

See, also, numbered paragraph 6 thereof, which reads as follows:

> "The mean chewing force is ***well below 500 N*** but high enough so that conventional pharmaceutical dosage forms ***<u>can</u> be crushed by chewing.*** Dosage forms having a breaking strength of at least 500 N, however, ***<u>cannot</u> be crushed by chewing*** (again, emphasis added)."

Oshlack's dosage forms are of the conventional type, and, indeed, Oshlack takes advantage of the fact that they can be crushed by chewing by incorporating into them aversive agents that release on that happenstance, discouraging the addict from taking additional steps to abuse the opioid contained therein.

Dr. Bartholomäus' conclusions regarding the chewing force are supported by the Prosechel article, of record, and, along with the evidence in that article, also stand unrebutted on the present record.

(b). Applicants have reproduced Oshlack's closest example, Example 16, and shown that it does not inherently lead to a dosage form having a breaking strength of at least 500 N, as presently claimed.

Indeed, Applicants have reproduced Oshlack's closest example, Example 16, and shown the resulting dosage form to have a breaking strength consistent with conventional dosage forms.

In this regard, Applicants refer once again to Dr. Bartholomäus' declaration executed August 25, 2008, and filed as an attachment to the amendment after final filed February 17, 2009.

Example 1 in the Table on page 2 of the declaration is Oshlack's Example 16 reproduced exactly except that hydromorphone HCl has been replaced by oxycodone

HCl. The reasons for the substitution are explained in numbered paragraph 4.2a on page 4 of the declaration. Most importantly, Dr. Bartholomäus testifies that:

> "This replacement of the active ingredient, however, does not alter the breaking strength of the thus obtained dosage form, i.e., the corresponding dosage form containing hydromorphone HCl instead of oxycodone HCl also has a breaking strength of substantially less than 500 N."

Indeed, the Examiner should note that the dosage form of Example 1 in the Table on page 2, which is, again, Oshlack's Example 16, exhibited a breaking strength of only **284 N**. This is consistent with Applicants' arguments and evidence that Oshlack's dosage forms are conventional dosage forms that can be crushed by chewing, and, therefore, do not have a breaking strength of at least 500 N, as required by the instant claims.

Example 2 in the declaration Table on page 2 is another embodiment within Oshlack's disclosure, but not a reproduction of an actual working example. Details about this particular example are given in paragraph 4.2b on page 4 of the declaration. Importantly, the resultant dosage form did not exhibit a breaking strength anywhere near at least 500 N, as required by the instant claims. Thus, this example also supports Applicants' declaration and literature evidence that Oshlack's dosage forms are conventional dosage forms intended to be crushed by chewing, which, therefore, do not have a breaking strength anywhere near at least 500 N, as required by the instant claims.

(c). The Examiner has not established that a person having ordinary skill in the art, substituting Dow's high molecular

weight PEO polymers into Oshlack's dosage forms would have expected to achieve a dosage form having a breaking strength of at least 500 N.

A person having ordinary skill in the art, expecting to prepare yet another Oshlack-type dosage form by using Dow's PEO polymers, would have expected, instead, to obtain another conventional dosage form that could be crushed by chewing consistent with Oshlack's teachings, and the declaration and literature evidence Applicants have provided. Such person would, furthermore, have expected that such newly obtained dosage form likewise would have functioned in accordance with Oshlack's disclosure, and, thus, could be crushed by chewing or other means ordinarily available to an addict, and when this occurred would also release its contained aversive agents, thereby discouraging the addict from taking further steps to abuse the opioid contained therein.

A person having ordinary skill in this art would not have expected to achieve the instant dosage form having a breaking strength of at least 500 N, a dosage form that was so strong that it could not be crushed by chewing or other means ordinarily available to the addict and, thus, could never release its aversive agents contained therein in the manner Oshlack contemplates. Nor would such person inherently have obtained the instant dosage form, once again for the reasons given above, and proven by the evidence of this record. Again, the data establish that it is entirely possible to take any of Dow's PEO polymers and operate within Oshlack's PEO:opioid ratio of 1:15 to 15:1 and ***not*** produce a dosage form exhibiting a breaking strength of at least 500 N, as required by the instant claims. Consequently, a breaking strength of at least 500 N is not inherent in either Oshlack alone or in the combined Oshlack/Dow teachings.

(d). Applicants production of a novel type of dosage form, one having a breaking strength of at least 500 N, which is, therefore, so strong that it cannot be crushed with a hammer, and, thus, provides abuse-proofing in an entirely novel manner, i.e., by virtue of extreme strength against breaking, is an unexpected result that cannot be gleaned from the combination of Oshlack and Dow, nor was its production inherent in such combination.

Since the person having ordinary skill in the art would not have expected, given Oshlack and Dow, to have achieved the instant dosage form having a breaking strength of at least 500 N, Applicants' production of such dosage form is surprising and unexpected. Further, since neither Oshlack alone nor Oshlack taken in combination with Dow teaches or suggests any benefits of a dosage form having a breaking strength of at least 500 N, yet such dosage forms have been discovered by Applicants to be useful to discourage opioid abuse in a novel and fundamentally different way than Oshlack, Applicants respectfully submit that the surprising and unexpected novelty of Applicants' dosage forms, and the new abuse-proof technology embodied therein, provide ample basis for grant of a patent.

i. The Examiner measures the present invention against the wrong target—the dosage form that *hypothetically would result* from the combined teachings of Oshlack and Dow.

The Examiner in her statement of the rejection writes, in numbered paragraph 15 on page 6, with reference to "the sustained release ***dosage forms of <u>the combined references</u>*** of [Oshlack] and [Dow] (emphasis added)" that:

> "If the prior art ***teaches*** the composition, then the properties are also taught by the prior art (emphasis added)."

Citation is made to *In re Spada,* 911 F.2d 705, 709, 15 USPQ2d 1655, 1658 (Fed. Cir. 1990); and *MPEP* § 2112.01.

This is apparently an inherency argument, which Applicants respectfully submit is not justified in the present case, as should already be clear to the Examiner from the discussion above.

Thus, in the very next sentence, the Examiner calls on Applicants to provide more evidence of some sort, the Examiner commenting:

> "The burden is shifted to Applicant to show that ***the prior art product*** does not possess or render obvious the same properties as the instantly claimed product as the instant claims do not provide ***the necessary limitations*** to distinguish the abuse proof dosage form over the prior art (again, emphasis added)."

Taking the issue of "necessary limitations" first, Applicants point out that, as noted above, the instant claims require "said component (C) [is] present in an amount sufficient to result in a breaking strength of said sintered mass of at least 500 N." Applicants respectfully submit that this limitation patentably distinguishes the instant dosage form from Oshlack's dosage forms, and provides ample basis for grant of the instant claims.

It is well settled that functional language can be distinguishing even at the point of novelty. *See, for example,* even the *Spada* case 15 USPQ2d at 1658, citing *E. I. DuPont de Nemours & Co. v. Phillips Petroleum Co.,* 849 F.2d 1430, 1435, 7 USPQ2d

1129, 1133 (Fed. Cir.), cert. denied, 109 S.Ct. 542 (1988), acknowledging that "newly discovered ***properties can*** be the basis of claims to ***novel*** polymers (emphasis added)." The present record is clear and establishes that Oshlack's dosage forms can be ***crushed by chewing*** and have a breaking strength ***far below*** 500 N, whereas the instant dosage forms ***cannot*** be crushed by chewing and have a breaking strength of ***at least 500 N.*** Consequently, the requirement of the instant claims that "said component (C) [is] present in an amount sufficient to result in a breaking strength of said sintered mass of at least 500 N" does, in fact, distinguish the instant dosage forms from Oshlack's dosage forms.

A problem with the Examiner's analysis is her treatment of the dosage form that would result from the combined teachings of Oshlack and Dow ***as already existing in the prior art.*** It does not. Rather, the dosage form that would result from the combined teachings of Oshlack and Dow is a hypothetical figment of the Examiner's imagination. It does not exist in the prior art, is not "taught" by the prior art, but is alleged merely to be "suggested" thereby. Thus, the Examiner's statement in the Office Action "[i]f the prior art teaches the composition, then the properties are also taught * * *" does not apply here, as the prior art does ***not teach*** the composition, but at best only ***suggests*** it.

Moreover, if the Examiner has done her job right in combining Oshlack and Dow, the dosage form ***that would result from the combined teachings*** of Oshlack and Dow ***is, in effect, the invention.*** And so, what the Examiner is really asking, when she asks that Applicants show that "the prior art product" does not possess the same properties as the instantly claimed product, is that ***Applicants distinguish their invention from***

their invention, which is not only impossible, but, thankfully, is not a valid requirement under the U.S. patent law.

A similar rationale was held by the examiner therein in the recent case of *Ex parte Hirata et al.*, 2009 WL 2142960 (BPAI 2009), a copy of which was enclosed for the Examiner's convenience. Applicant therein attempted to show the unexpected benefit of the invention claimed therein over an embodiment of the closest prior art reference. The examiner therein criticized the showing, the Board noting the following:

> "The Examiner only asserts that this showing is not sufficient since it is not directed to ***a comparison between the claimed invention and the invention suggested by the combined teachings of the prior art references.*** However, we know of no legal precedent for such a requirement. ***Appellants cannot be required to compare the invention against itself*** (emphasis added)."

See the first paragraph on page 8 of the decision. At the top of the previous page, the Board advanced the following principles of law:

> "When an obviousness rejection is based on a combination of the prior art references, the comparison ***need only be between the closest prior art reference and the claimed invention.*** *In re Baxter Travenol Labs.*, 952 F.2d 388, 392 (Fed. Cir. 1991); *In re Chapman*, 357 F.2d 418, 422 (CCPA 1966). ***It need not be directed to a comparison between the claimed invention and the invention suggested by the combined teachings of the prior art references.*** *Chapman*, 357 F.2d at 422 (again, emphasis added)."

Applicants believe the decision in *In re Chapman* is especially pertinent. There, product claims were at issue, and the Examiner made findings there *similar to those involved herein,* the Examiner's Answer therein stating:

> "It is deemed that in view of the similarity in preparation, the claimed polymers ***must*** be the same as the Noeske polymers except for properties that are the result of treating a higher molecular weight starting material (emphasis added)."

See, Chapman, 357 F.2d at 421. According to the Court, the Board of Appeals in its decision added:

> "[T]he affidavit is silent as to the results obtained when the high molecular weight polyethylene of [the secondary reference] Hoerger et al. is ***substituted*** for the polyethylene of [the primary reference] Noeske. This is the essence of the Examiner's rejection and ***it would appear that such a substitution would inherently yield a product substantially the same as that claimed*** (emphasis added)."

See, Chapman, 357 F.2d at 422.

The examiner's/Board's rationale in *Chapman* is substantially identical to the Examiner's rationale here: That is, by analogy, substitution of the higher molecular weight materials of Dow into the dosage forms of Oshlack would inherently yield a dosage form substantially as presently claimed.

The Court struck down such rationale as being invalid, holding as follows:

> ***"We do not agree*** with the board that a high molecular weight polyethylene of [the secondary reference] Hoerger should have been substituted for the polyethylene of [the primary reference] Noeske if comparative data are to be presented ***for this, we think, would amount to requiring comparison of the results of the invention with the results of the invention.*** Nor can we agree that appellants' compositions are unpatentable because such a process 'would inherently yield' a product substantially the same as that claimed, since that position implies that any and all products of obvious processes are unpatentable by reason of their being the 'inherent' results of those processes (again, emphasis added)."

Id.

ii. The properties of the inventive dosage form vis-à-vis those of Oshlack's closest working example represent the proper comparison, and such comparison shows the inventive dosage forms have unexpectedly different significant properties.

Spada is easily distinguished on its facts from the instant case. *Spada* was a case of ***anticipation*** in that the exact compound claimed, not some close relative thereof requiring modification, was taught/known in the prior art. *See, Spada,* 15 USPQ2d at 1657 ("The Board held that the compositions claimed by Spada 'appear to be ***identical'*** to those described by Smith"); and at 1658 ("[W]hen the PTO shows sound basis for believing that the products of the applicant and the prior art ***are the same,*** the applicant has the burden of showing that they are not. * * * Spada offered no such showing.") Inasmuch as "a compound and all its properties are inseparable;

they are one and the same thing" (*In re Papesch,* 137 USPQ 43, 51 (CCPA 1963)), the disclosure of the identical compound in the prior art was justly found in *Spada* to be an inherent disclosure of the newly discovered properties applicants therein claimed. Newly discovered properties of an old composition cannot confer patentability on the composition itself.

However, the present case is altogether different, as the inventive dosage forms are ***conceded to be novel;*** the Examiner does not allege that any single prior art reference ***teaches*** the inventive dosage forms, but only that a combination of prior art references ***suggest*** the inventive dosage forms. In such a case, where the claims relate to novel products, even *Spada* acknowledges that differences in properties can be the basis for patentability. *See, again, Spada,* 15 USPQ2d at 1658, citing *E. I. DuPont de Nemours & Co. v. Phillips Petroleum Co.,* 849 F.2d 1430, 1435, 7 USPQ2d 1129, 1133 (Fed. Cir.), cert. denied, 109 S.Ct. 542 (1988), for the proposition that "newly discovered ***properties can*** be the basis of claims to ***novel*** polymers (emphasis added)."

Where, as here, the Examiner pieces together bits from a combination of references to form a hypothetical product, and alleges that the newly conjured product would have been obvious to persons having ordinary skill in the particular art involved given that combination of references, applicants have always be able to prove that the new product, once applicants actually made it, exhibited properties that could not have been expected and did not exist in the closest products of the closest of the combined references. And, if such unexpected difference in properties is proven, and the properties are of practical significance, then it has always been the case that the patent

will issue in spite of the fact that at first blush the compound appeared to have been obvious. *See, again, Papesch,* 137 USPQ at 51:

> "From the standpoint of patent law, a compound and all of its properties are inseparable; they are one and the same thing. The graphic formulae, the chemical nomenclature, the systems of classification and study such as the concepts of homology, isomerism, etc., are mere symbols by which compounds can be identified, classified and compared. But a formula is not a compound and while it may serve in a claim to *identify* what is being patented, as the metes and bounds of a deed identify a plot of land, the *thing* that is patented is not the formula but the compound identified by it. And the patentability of the thing does not depend on the similarity of its formula to that of another compound but of the similarity of the former compound to the latter. ***There is no basis in law for ignoring any property in making such a comparison. An assumed similarity*** based on a comparison of formulae ***must give way to evidence that the assumption is erroneous.*** [Plain italics in original and bold italics added.]"

Such is the case here: The Examiner's assumption that Dow's PEO polymers could be substituted into Oshlack's dosage form to produce yet another dosage form similar to those described by Oshlack itself must give way to the evidence already of record that Applicants' novel products have breaking strength properties not found in any of Oshlack's dosage forms, which different breaking strength properties allow the new materials to be used to combat opioid abuse in a fundamentally new and different manner than Oshlack envisions. Consistent with Applicants' arguments, as noted above, they have reproduced Example 16 of Oshlack's disclosure (see, again, Example

1 of Dr. Bartholomäus' declaration executed August 25, 2008, and filed as an attachment to the amendment after final filed February 17, 2009). This reproduced Example 16 provides evidence as to the general nature of the properties that persons skilled in the art could have expected of Oshlack's dosage forms. Such dosage form is proven to have a breaking strength of only 284 N, consistent with it being crushable by chewing, which would allow release of the aversive agents contained therein, leading the addict to be discouraged from taking further steps to abuse the opioid contained therein. As such, this reproduced Example 16 is capable of functioning in exactly the manner Oshlack describes in his disclosure.

In stark contrast to this, the inventive dosage forms are shown in a myriad of comparison examples to have completely different properties altogether. They are shown to have breaking strengths above 500 N. The inventive dosage forms are not crushable by chewing, as are Oshlack's dosage forms, but, instead, are so strong that they cannot be broken open even with a hammer. As such, the inventive dosage forms are simply incapable of operating in the manner Oshlack contemplates, i.e., by chewing or crushing with means ordinarily available to the addict thereby to release the aversive agents contained therein, which aversive agents, when released, discourage the addict from taking further steps in the abuse of the opioid contained therein. Instead, with the inventive dosage form, abuse is discouraged in a fundamentally different way. The difference is not a difference in degree, but quite literally a difference in kind. The inventive dosage forms are simply so strong that an addict cannot by ordinary means available to them chew, break or crush them, and so cannot gain access to the opioid contained therein.

There is nothing in Oshlack alone or in combination with Dow that teaches or suggests dosage forms having a breaking strength of at least 500 N, or the practical usefulness of such materials in discouraging opioid abuse. Accordingly, Applicants have demonstrated by way of the numerous declarations of record that such materials can not only be obtained, but are also of practical benefit in curbing opioid abuse, opening up an entirely new methodology for fighting such abuse, namely extreme dosage form breaking strength, render the dosage form non-crushable. Applicants respectfully submit that their demonstration of all these differences from the Oshlack dosage forms and the advantages thereover must be considered to be surprising and unexpected results and, therefore, also objective evidence of nonobviousness.

Applicants' claims cannot therefore be seen as obvious over the disclosure of Oshlack, and the rejection of claims 1, 2, 4, 7, 8, 27-29, 31, 41 and 42 under 35 U.S.C. 103(a) as obvious over Oshlack et al (US 2003/0064099/A1) in view of DOW Technical Data, POLYOX^{TM} WSR, February 2003, should now be withdrawn.

In view of the present amendments and remarks it is believed that claims 1, 2, 4, 7, 8, 27-29, 31, 41 and 42 are now in condition for allowance. Reconsideration of said claims by the Examiner is respectfully requested and the allowance thereof is courteously solicited.

CONDITIONAL PETITION FOR EXTENSION OF TIME

If any extension of time for this response is required, Applicants request that this be considered a petition therefor. Please charge the required petition fee to Deposit Account No. 14-1263.

ADDITIONAL FEE

Please charge any insufficiency of fee or credit any excess to Deposit Account No. 14-1263.

Respectfully submitted,
NORRIS, McLAUGHLIN & MARCUS, PA

By /William C. Gerstenzang/
William C. Gerstenzang
Reg. No. 27,552

WCG/tmo
875 Third Avenue - 8th Floor
New York, New York 10022
(212) 808-0700